V. Balasubramanian

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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	Jan 25	BLAST(R) searching in REGISTRY available in STN on the Web
NEWS	3	Jan 29	FSTA has been reloaded and moves to weekly updates
NEWS	4	Feb 01	DKILIT now produced by FIZ Karlsruhe and has a new update frequency
NEWS	5	Feb 19	Access via Tymnet and SprintNet Eliminated Effective 3/31/02
NEWS	6	Mar 08	Gene Names now available in BIOSIS
NEWS	7	Mar 22	TOXLIT no longer available
NEWS	8	Mar 22	TRCTHERMO no longer available
NEWS	9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
NEWS	10	Mar 28	LIPINSKI/CALC added for property searching in REGISTRY
NEWS	11	Apr 02	PAPERCHEM no longer available on STN. Use PAPERCHEM2 instead.
NEWS	12	Apr 08	"Ask CAS" for self-help around the clock
NEWS	13	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS	14	Apr 09	ZDB will be removed from STN
NEWS	15	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS	16	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS	17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS	18	Apr 22	Federal Research in Progress (FEDRIP) now available

NEWS EXPRESS	February 1 CURRENT WINDOWS VERSION IS V6.0d, CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP), AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:24:53 ON 06 MAY 2002

V. Balasubramanian

```
=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 16:24:58 ON 06 MAY 2002
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STRUCTURE FILE UPDATES:    5 MAY 2002  HIGHEST RN 411206-65-0
DICTIONARY FILE UPDATES:   5 MAY 2002  HIGHEST RN 411206-65-0

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 10050488.str

L1      STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1                STR
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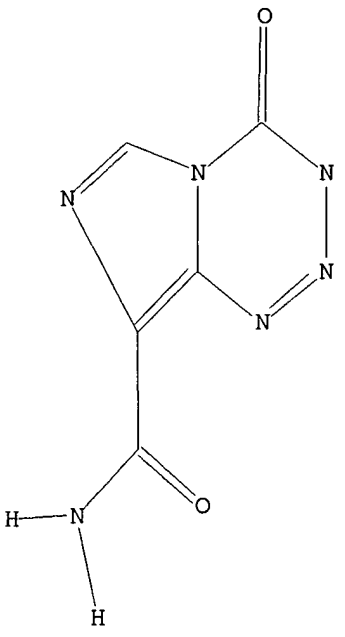


V. Balasubramanian

Structure attributes must be viewed using STN Express query preparation.

```
=> s l1 sss sam
SAMPLE SEARCH INITIATED 16:25:25 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      9 TO ITERATE

100.0% PROCESSED       9 ITERATIONS                              3 ANSWERS
SEARCH TIME: 00.00.01

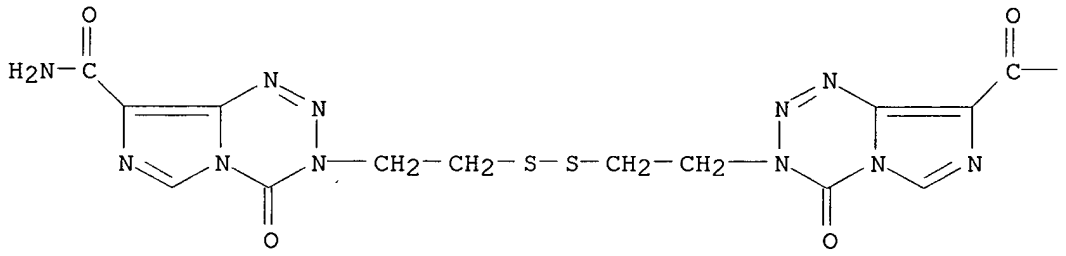
FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            9 TO      360
PROJECTED ANSWERS:               3 TO      163

L2            3 SEA SSS SAM L1

=> d scan

L2   3 ANSWERS   REGISTRY  COPYRIGHT 2002 ACS
IN   Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-(dithiodi-2,1-
     ethanediyl)bis[3,4-dihydro-4-oxo- (9CI)
MF   C14 H14 N12 O4 S2
```

PAGE 1-A



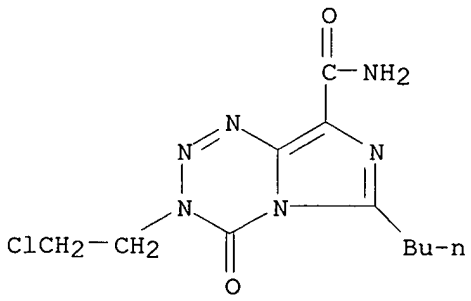
PAGE 1-B

—NH_2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

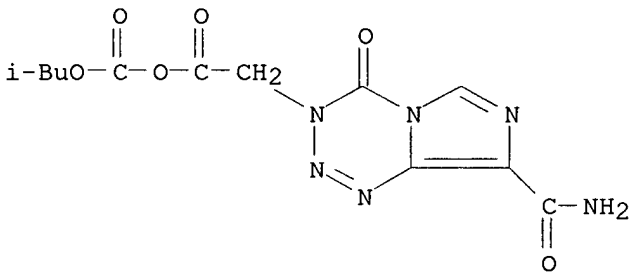
```
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L2   3 ANSWERS   REGISTRY  COPYRIGHT 2002 ACS
IN   Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 6-butyl-3-(2-chloroethyl)-
     3,4-dihydro-4-oxo- (9CI)
MF   C11 H15 Cl N6 O2
```



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 3 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Imidazo[5,1-d]-1,2,3,5-tetrazine-3(4H)-acetic acid, 8-(aminocarbonyl)-4-oxo-, anhydride with 2-methylpropyl hydrogen carbonate (9CI)
MF C12 H14 N6 O6



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> s l1 sss ful
FULL SEARCH INITIATED 16:25:53 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 186 TO ITERATE

100.0% PROCESSED 186 ITERATIONS 66 ANSWERS
SEARCH TIME: 00.00.01

L3 66 SEA SSS FUL L1

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	140.66	140.87

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```
FILE 'REGISTRY' ENTERED AT 16:26:00 ON 06 MAY 2002
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DICTIONARY FILE UPDATES:   5 MAY 2002  HIGHEST RN 411206-65-0

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> s l3
SAMPLE SEARCH INITIATED 16:26:08 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      9 TO ITERATE

100.0% PROCESSED       9 ITERATIONS                              3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            9 TO      360
PROJECTED ANSWERS:               3 TO      163

L4            3 SEA SSS SAM L1

=> d l4 1-3 bib abs hitstr
'BIB' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'ABS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual
fields or predefined formats.  The predefined substance formats
are:  (RN = CAS Registry Number)

REG    - RN
SAM    - Index Name, MF, and structure - no RN
FIDE   - All substance data, except sequence data
IDE    - FIDE, but only 50 names
SQIDE  - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD    - Protein sequence data, includes RN
SQD3   - Same as SQD, but 3-letter amino acid codes are used
SQN    - Protein sequence name information, includes RN

CALC   - Table of numeric properties
PROP   - Same as CALC
```

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS --ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ENTER DISPLAY FORMAT (IDE):end

=> d l4 1-3 bib abs hitstr
'BIB' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'ABS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

REG - RN
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SQIDE - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD - Protein sequence data, includes RN
SQD3 - Same as SQD, but 3-letter amino acid codes are used
SQN - Protein sequence name information, includes RN

CALC - Table of numeric properties
PROP - Same as CALC

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
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IABS --ABS, indented, with text labels
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SIBIB ------- IBIB, no citations

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The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

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HELP FORMATS -- To see detailed descriptions of the predefined formats.
Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ENTER DISPLAY FORMAT (IDE):end

=> d l4 1-3 bib hitstr abs
'BIB' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'ABS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

REG - RN
SAM - Index Name, MF, and structure - no RN
FIDE - All substance data, except sequence data
IDE - FIDE, but only 50 names
SQIDE - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD - Protein sequence data, includes RN

SQD3 - Same as SQD, but 3-letter amino acid codes are used
SQN - Protein sequence name information, includes RN

CALC - Table of numeric properties
PROP - Same as CALC

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS --ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ENTER DISPLAY FORMAT (IDE):end

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.90	142.77

FILE 'CAPLUS' ENTERED AT 16:28:48 ON 06 MAY 2002
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FILE COVERS 1907 - 6 May 2002 VOL 136 ISS 19
FILE LAST UPDATED: 3 May 2002 (20020503/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

```
=> s l3
L5          295 L3

=> s l5/prep
FIELD CODES CANNOT BE CHANGED HERE
You may have tried to apply a field code to a term that already has a
field code.  You can only add a field code to a term that has no field
code appended to it.

=> s l3/prep
            295 L3
        2860177 PREP/RL
L6           17 L3/PREP
                   (L3 (L) PREP/RL)

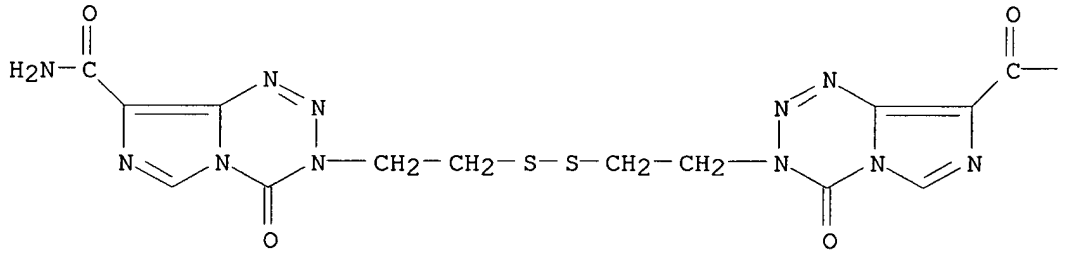
=> d l6 1-17 bib abs hitstr
```

L6 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 2000:887417 CAPLUS
DN 134:252318
TI Antitumor imidazotetrazines. Part 39. Synthesis of bis(imidazotetrazine)s with saturated spacer groups
AU Arrowsmith, Jill; Jennings, Sharon A.; Langnel, David A. F.; Wheelhouse, Richard T.; Stevens, Malcolm F. G.
CS Cancer Research Laboratories, School of Pharmaceutical Sciences, University of Nottingham, University Park, Nottingham, NG7 2RD, UK
SO Perkin 1 (2000), (24), 4432-4438
CODEN: PERKF9; ISSN: 1470-4358
PB Royal Society of Chemistry
DT Journal
LA English
AB Bis(imidazotetrazine)s, related in structure to the antitumor agents mitozolomide and temozolomide, but linked through the N(3)-N(3') atoms of the imidazo[5,1-d][1,2,3,5]tetrazine ring-systems, are prepd. by interaction of 5-diazoimidazole-4-carboxamide and diisocyanates. The presence of the polymethylene linker with/without sulfur and oxygen hetero atoms does not substantially affect the acid stability, base-catalyzed decompn., antitumor activity or DNA base alkylation preference characteristic of the unlinked imidazotetrazines mitozolomide and temozolomide.
IT **331456-52-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(prepn. and antitumor activity of (alkanediyl)bis[imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide] derivs.)

RN 331456-52-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-(dithiodi-2,1-ethanediyl)bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

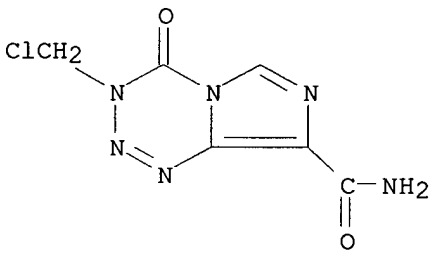


PAGE 1-B

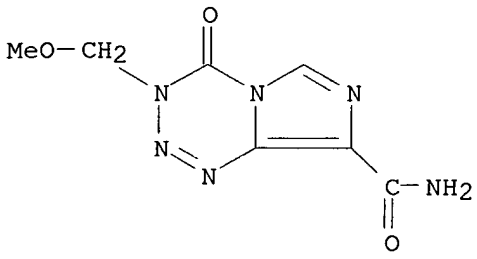
—NH_2

IT **331456-36-1P 331456-37-2P 331456-38-3P**
331456-39-4P
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of)

RN 331456-36-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(chloromethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



RN 331456-37-2 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-(methoxymethyl)-4-oxo- (9CI) (CA INDEX NAME)



RN 331456-38-3 CAPLUS
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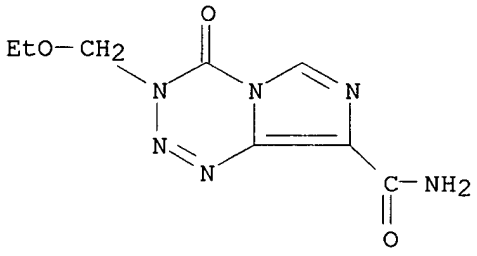
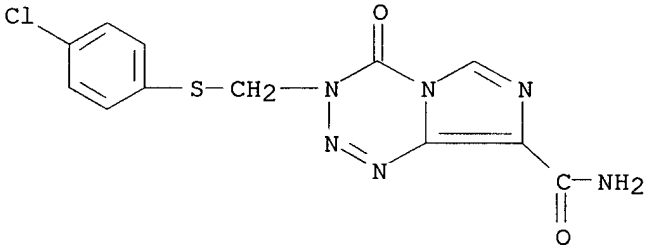
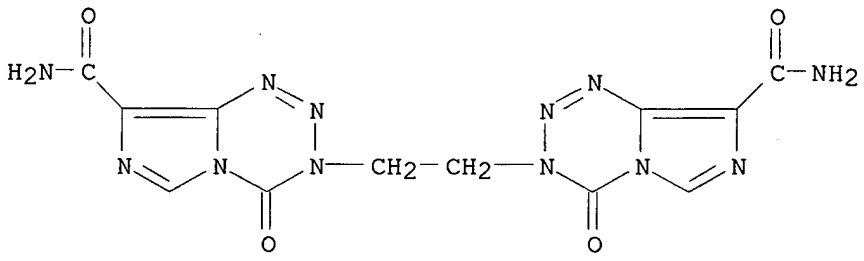


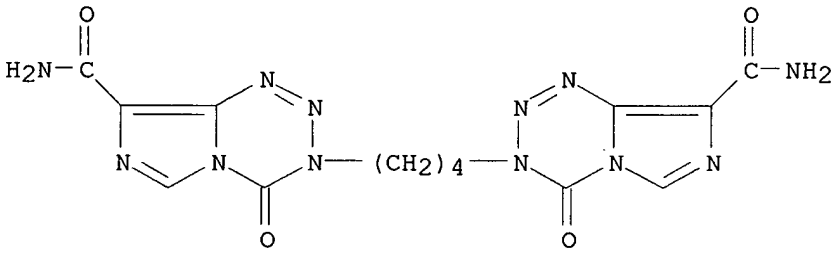
RN 331456-39-4 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-[[(4-chlorophenyl)thio]methyl]-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



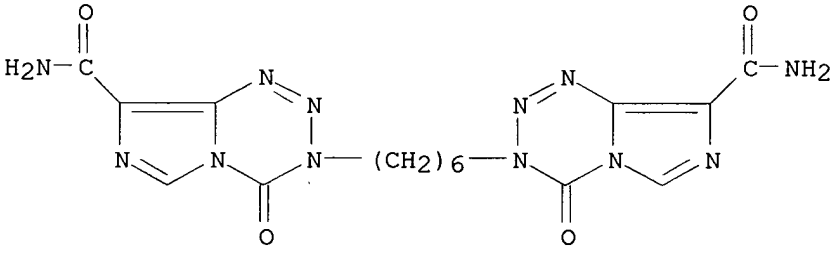
IT **331456-41-8P 331456-42-9P 331456-43-0P**
331456-44-1P 331456-45-2P 331456-46-3P
331456-47-4P 331456-48-5P 331456-49-6P
331456-50-9P 331456-51-0P
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of (alkanediyl)bis[imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide] derivs.)
RN 331456-41-8 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-(1,2-ethanediyl)bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



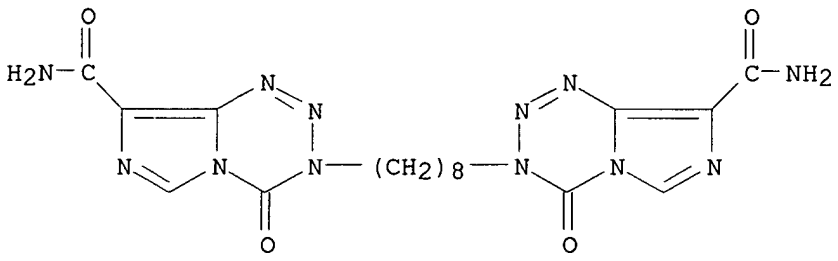
RN 331456-42-9 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-(1,4-butanediyl)bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



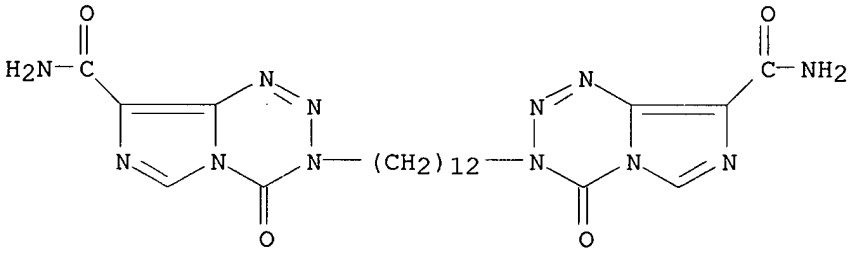
RN 331456-43-0 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-(1,6-hexanediyl)bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



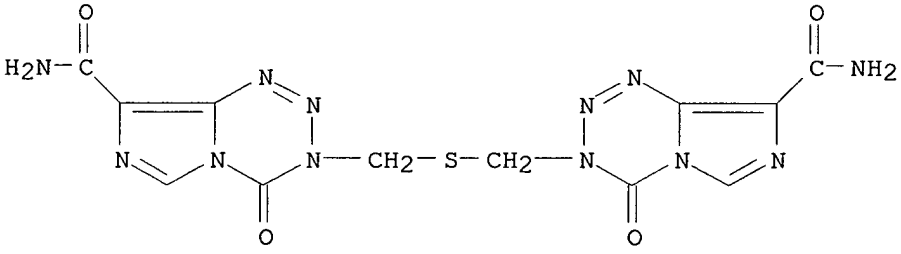
RN 331456-44-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-(1,8-octanediyl)bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



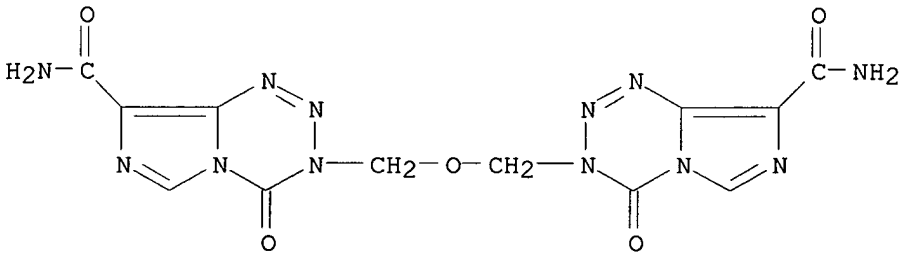
RN 331456-45-2 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-(1,12-dodecanediyl)bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



RN 331456-46-3 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-[thiobis(methylene)]bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)

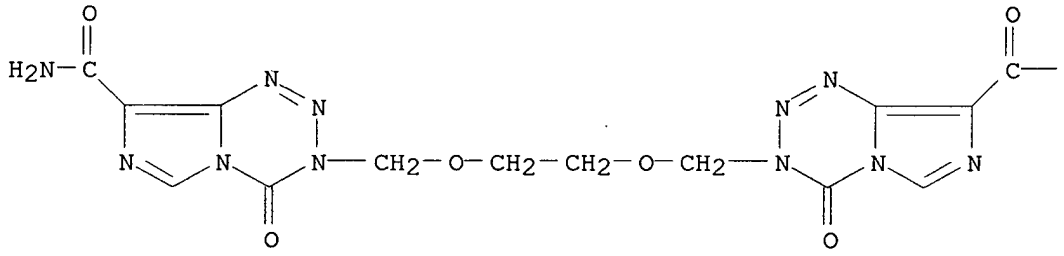


RN 331456-47-4 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-[oxybis(methylene)]bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



RN 331456-48-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-[1,2-ethanediylbis(oxymethylene)]bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

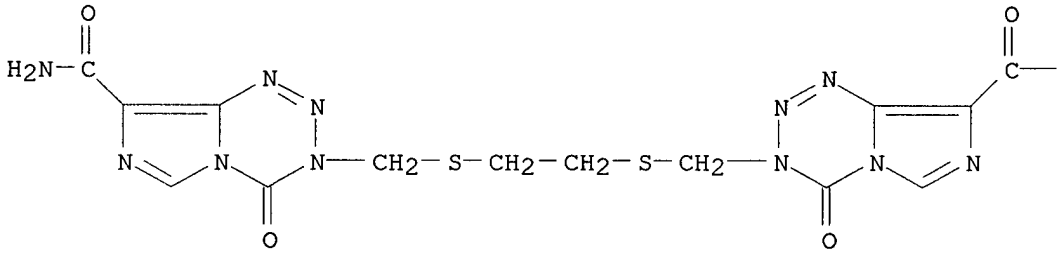


PAGE 1-B

—NH2

RN 331456-49-6 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-[1,2-ethanediylbis(thiomethylene)]bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)

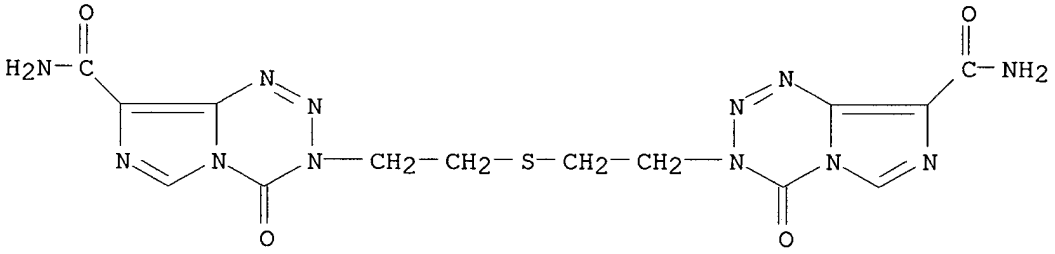
PAGE 1-A



PAGE 1-B

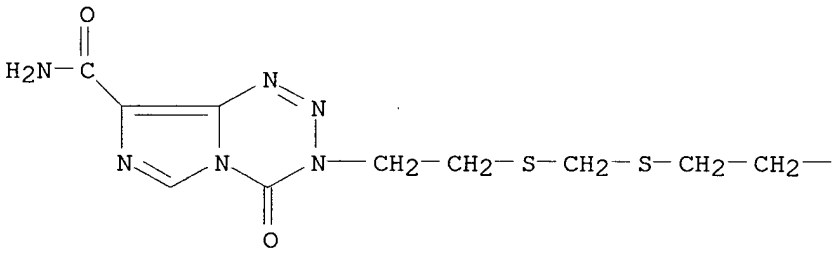
—NH_2

RN 331456-50-9 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-(thiodi-2,1-ethanediyl)bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)

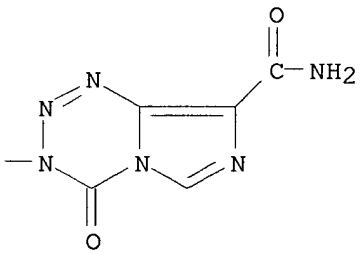


RN 331456-51-0 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-[methylenebis(thio-2,1-ethanediyl)]bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

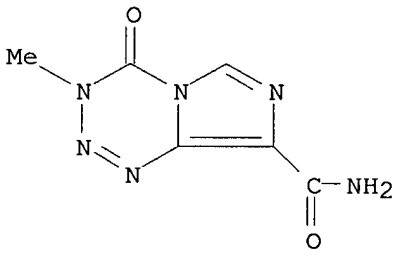


RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2002 ACS

V. Balasubramanian

AN 1999:794749 CAPLUS
DN 132:151791
TI Pyrrolo[2,1-d][1,2,3,5]tetrazines, a new class of azolotetrazines related to the antitumor drug temozolomide
AU Diana, Patrizia; Barraja, Paola; Lauria, Antonino; Almerico, Anna Maria; Dattolo, Gaetano; Cirrincione, Girolamo
CS Dipartimento Farmacochimico-Tossicologico Biologico, Univ. Studi Palermo, Palermo, I-90123, Italy
SO Synthesis (1999), (12), 2082-2086
CODEN: SYNTBF; ISSN: 0039-7881
PB Georg Thieme Verlag
DT Journal
LA English
OS CASREACT 132:151791
AB A series of pyrrolo[2,1-d][1,2,3,5]tetrazines, potential antineoplastic agents, was obtained in good yield from the reaction of 2-diazopyrroles with isocyanates at room temp. and in the dark. At. charges at C(4), a good parameter to predict the antineoplastic activity for this type of compds., are very close to that of temozolomide.
IT **85622-93-1P**, Temozolomide
RL: PNU (Preparation, unclassified); **PREP (Preparation)**
(prepn. and at. charge of pyrrolo[2,1-d][1,2,3,5]tetrazines related to temozolomide)
RN 85622-93-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

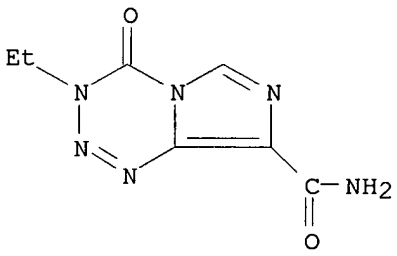
L6 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1998:259743 CAPLUS
DN 129:27924
TI Antitumor imidazotetrazines. Part 36. Conversion of 5-aminoimidazole-4-carboxamide to imidazo[5,1-d][1,2,3,5]tetrazin-4(3H)-ones and imidazo[1,5-a][1,3,5]triazin-4(3H)-ones related in structure to the antitumor agents temozolomide and mitozolomide
AU Wang, Yongfeng; Wheelhouse, Richard T.; Zhao, Linxiang; Langnel, David A. F.; Stevens, Malcolm F. G.
CS School of Pharmaceutical Sciences, Cancer Research Laboratories, Nottingham University, Nottingham, NG7 2RD, UK
SO J. Chem. Soc., Perkin Trans. 1 (1998), (10), 1669-1675
CODEN: JCPRB4; ISSN: 0300-922X
PB Royal Society of Chemistry
DT Journal
LA English

V. Balasubramanian

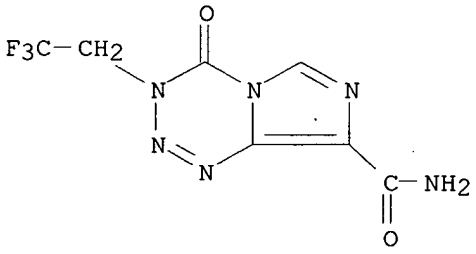
AB Novel 3-substituted imidazo[5,1-d][1,2,3,5]tetrazinones have been prepd. by two routes: reaction of 5-diazoimidazole-4-carboxamide and isocyanates, and nitrosative cyclization of 5-amino-1-carbamoylimidazole-4-carboxamides. The latter cyclizations do not proceed efficiently when the 1-carbamoyl group bears an electron-donating alkyl group. 5-Amino-1-carbamoylimidazole-4-carboxamides cyclize with tri-Et orthoformate or tri-Et orthobenzoate to yield imidazo[1,5-a][1,3,5]triazinones. A 1H NMR study of the decompn. of 8-carbamoyl-3-ethylimidazo[5,1-d][1,2,3,5]tetrazin-4(3H)-one in deuteriated phosphate buffer has shown that its ethylating capacity is attenuated by the unproductive generation of ethene. This observation explains why the ethylimidazotetrazine possesses weaker antitumor properties than the clin.-used congener temozolomide.

IT **97716-74-0P 208107-15-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of imidazo[5,1-d][1,2,3,5]tetrazin-4(3H)-ones and imidazo[1,5-a][1,3,5]triazin-4(3H)-ones)

RN 97716-74-0 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-ethyl-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)

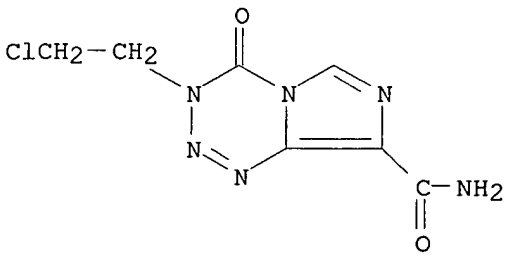


RN 208107-15-7 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-(2,2,2-trifluoroethyl)- (9CI) (CA INDEX NAME)

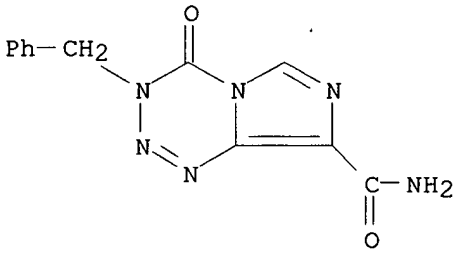


IT **85622-95-3P**, Mitozolomide **85623-02-5P**
208107-14-6P 208107-16-8P 208107-17-9P
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of imidazo[5,1-d][1,2,3,5]tetrazin-4(3H)-ones and imidazo[1,5-a][1,3,5]triazin-4(3H)-ones)

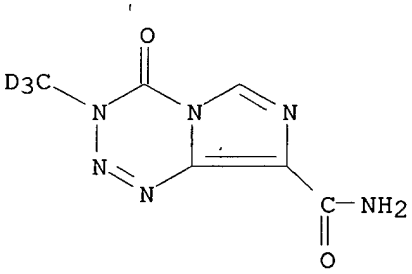
RN 85622-95-3 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



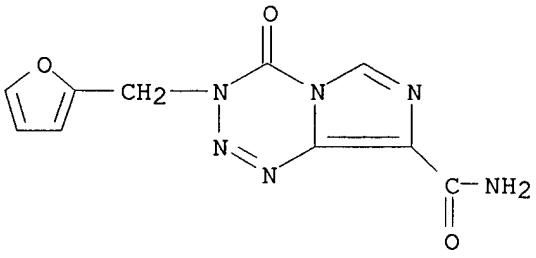
RN 85623-02-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



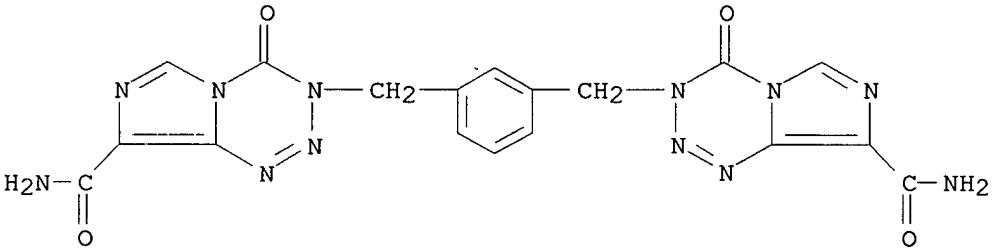
RN 208107-14-6 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-(methyl-d3)-4-oxo- (9CI) (CA INDEX NAME)



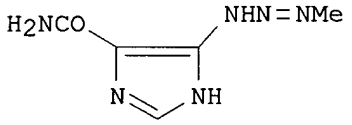
RN 208107-16-8 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-furanylmethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



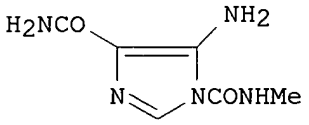
RN 208107-17-9 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,3'-[1,3-phenylenebis(methylene)]bis[3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



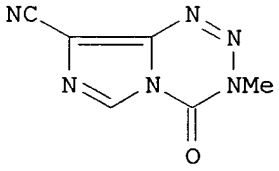
L6 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1997:684618 CAPLUS
DN 127:293195
TI Antitumor Imidazotetrazines. 35. New Synthetic Routes to the Antitumor Drug Temozolomide
AU Wang, Yongfeng; Stevens, Malcolm F. G.; Chan, Tze-ming; DiBenedetto, Donald; Ding, Zhe-xing; Gala, Dinesh; Hou, Donald; Kugelman, Max; Leong, William; Kuo, Shen-chun; Mas, Janet L.; Schumacher, Doris P.; Shutts, Bruce P.; Smith, Lyman; Zhan, Zheng-Yun J.; Thomson, William T.
CS Cancer Research Laboratories Department of Pharmaceutical Sciences, University of Nottingham, Nottingham, NG7 2RD, UK
SO J. Org. Chem. (1997), 62(21), 7288-7294
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
GI



II



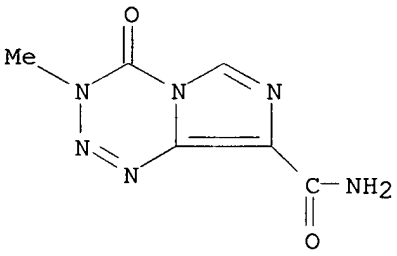
III



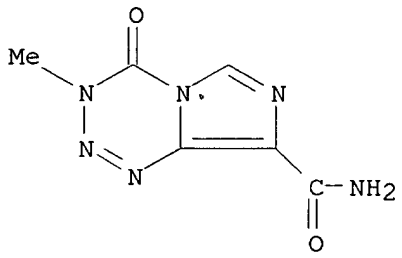
IV

AB Three new pathways to the antitumor drug temozolomide (I) were explored via intermediate imidazolecarboxamides II and III and the imidazotetrazinone IV. The key intermediate III was converted to I in 45% yield by employing NaNO2 in aq. tartaric acid at 0-5.degree.. III was prepd. from 5-amino-1-[[(4-nitrophenyl)oxy]carbonyl]imidazole-4-carboxamide and MeNH2 or directly from 5-aminoimidazole-4-carboxamide and either MeNCO or MeNHCOCl. I was also prepd. from IV by hydrolysis to the HCl salt of I in 10 M HCl. IV was prepd. from either 5-diazoimidazole-4-carbonitrile and MeNCO or by diazotization of 5-amino-1-(N-methylcarbamoyl)imidazole-4-carbonitrile. Attempts to cyclize II with phosgene or phosgene equiv. were unsuccessful and only 2-azahypoxanthine was isolated.

IT **85622-93-1P**, Temozolomide
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of temozolomide by cyclization of imidazolecarboxamides)
RN 85622-93-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)

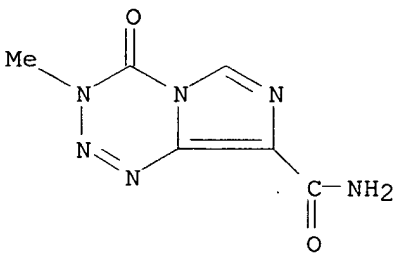


IT **196806-18-5P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of temozolomide hydrochloride by hydrolysis of cyanotemozolomide)
RN 196806-18-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

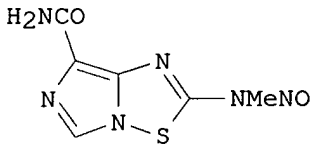
L6 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1997:417852 CAPLUS
DN 127:89996
TI Temozolomide: a review of its discovery, chemical properties, pre-clinical development and clinical trials
AU Newlands, E. S.; Stevens, M. F. G.; Wedge, S. R.; Wheelhouse, R. T.; Brock, C.
CS Dep. Med. Oncology, Charing Cross Hospital, London, W6 8RF, UK
SO Cancer Treat. Rev. (1997), 23(1), 35-61
CODEN: CTREDJ; ISSN: 0305-7372
PB Saunders
DT Journal; General Review
LA English
AB A review with 106 refs. on the synthesis of, mechanism of antitumor activity of and clin. trials with temozolomide.
IT **85622-93-1P**, Temozolomide.
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(temozolomide: discovery, chem. properties, pre-clin. development and clin. trials)
RN 85622-93-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



L6 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1997:168958 CAPLUS
DN 126:264081
TI A new route to the antitumor drug temozolomide, but not thiotemozolomide

V. Balasubramanian

AU Wang, Yongfeng; Lowe, Philip R.; Thomson, William T.; Clark, Jonathan; Stevens, Malcolm F. G.
CS Cancer Res. Lab., Univ. Nottingham, Nottingham, NG7 2RD, UK
SO Chem. Commun. (Cambridge) (1997), (4), 363-364
CODEN: CHCOFS; ISSN: 1359-7345
PB Royal Society of Chemistry
DT Journal
LA English
OS CASREACT 126:264081
GI

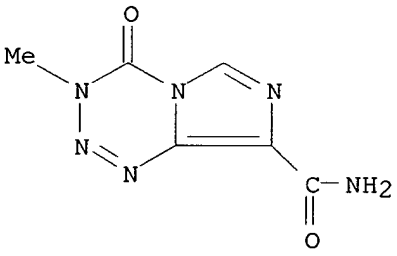


I

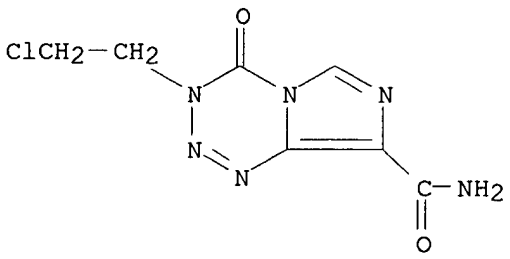
AB Interaction of 5-aminoimidazole-4-carboxamide with alkyl isocyanates yields N-substituted 1-carbamoylimidazoles which can be cyclized to imidazo[5,1-d][1,2,3]tetrazin-4(3H)-ones, including temozolomide, on nitrosation; a similar reaction with Me isothiocyanate, followed by nitrosation, affords the nitrosomethylamino deriv. I of a new ring-system, imidazo[1,5-b][1,2,4]thiadiazole.

IT **85622-93-1P 85622-95-3P 85623-02-5P**
97716-74-0P
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of temozolomide and imidazo[1,5-b][1,2,4]thiadiazole deriv.)

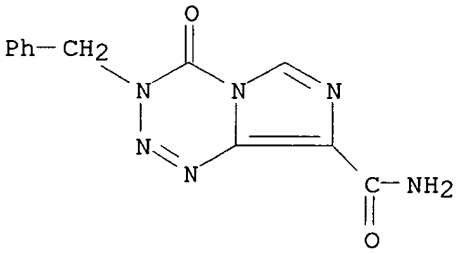
RN 85622-93-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



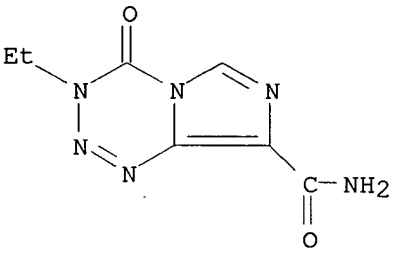
RN 85622-95-3 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



RN 85623-02-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



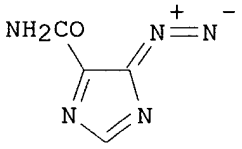
RN 97716-74-0 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-ethyl-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



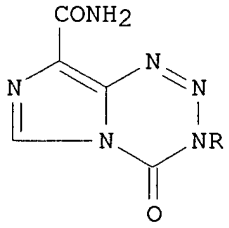
L6 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1996:108643 CAPLUS
DN 124:232405
TI Synthetic studies of 8-carbamoylimidazo-[5,1-D]-1,2,3,5-tetrazin-4(3H)-one: a key derivative of antitumor drug temozolomide
AU Wang, Yongfeng; Stevens, Malcolm F. G.
CS Cancer Res. Campaign Experimental Cancer Chemotherapy Res. Group, Univ. Nottingham, Nottingham, NG7 2RD, UK
SO Bioorg. Med. Chem. Lett. (1996), 6(2), 185-8
CODEN: BMCLE8; ISSN: 0960-894X
DT Journal
LA English
OS CASREACT 124:232405

V. Balasubramanian

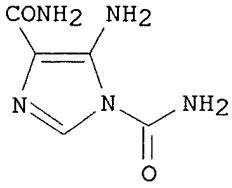
GI



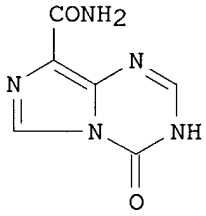
I



II



III



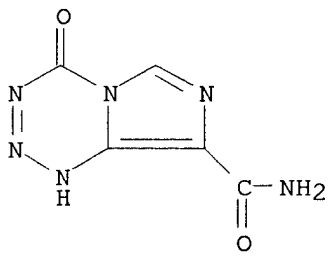
IV

AB 5-Diazoimidazole-4-carboxamide (I) reacted with trimethylsilyl isocyanate in acetonitrile to afford 8-carbamoylimidazo[5,1-d]1,2,3,5-tetrazin-4(3H)-one (II; R = H), which was undergoing a methylation to give antitumor drug temozolomide (II; R = Me); while 1,5-dicarbamoylaminoimidazole (III) failed in an azo-cyclization to give II (R = H) but accomplished a carbon-cyclization to produce 8-carbamoylimidazo[1,5-a] s-triazin-4(3H)-one (IV).

IT **108030-65-5P**, Nortemozolomide
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**
(synthetic studies with carbamoylimidazotetrazinone)

RN 108030-65-5 CAPLUS

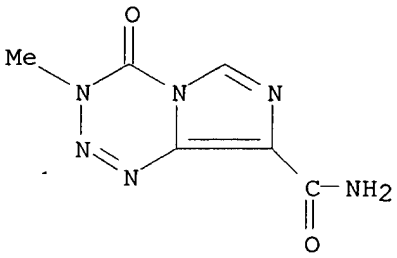
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 1,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



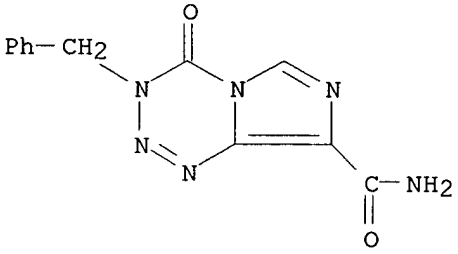
IT **85622-93-1P**, Temozolomide **85623-02-5P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(synthetic studies with carbamoylimidazotetrazinone)

RN 85622-93-1 CAPLUS

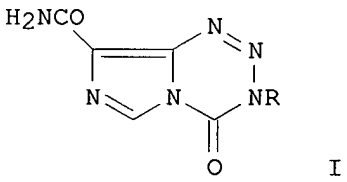
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



RN 85623-02-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



L6 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1995:933775 CAPLUS
DN 124:117266
TI Antitumor imidazotetrazines. Part 33. New syntheses of the antitumor drug temozolomide using 'masked' methyl isocyanates
AU Wang, Yongfeng; Stevens, Malcolm F. G.; Thomson, William T.; Shutts, Bruce P.
CS Cancer Res. Lab., Dep. Pharmaceutical Sci., Univ. Nottingham, Nottingham, NG7 2RD, UK
SO J. Chem. Soc., Perkin Trans. 1 (1995), (21), 2783-7
CODEN: JCPRB4; ISSN: 0300-922X
DT Journal
LA English
OS CASREACT 124:117266
GI



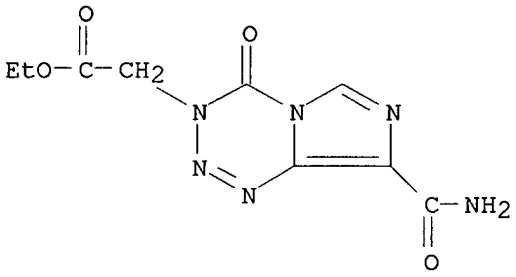
I

AB The imidazotetrazinylacetate I [R = CH2CO2Et] can be prepd. by treating 5-diazoimidazole-4-carboxamide with Et isocyanatoacetate or by diazotization of N-(5-amino-4-carbamoylimidazol-1-ylcarbonyl)glycine Et ester. Hydrolysis to the acid and Barton radical decarboxylation affords

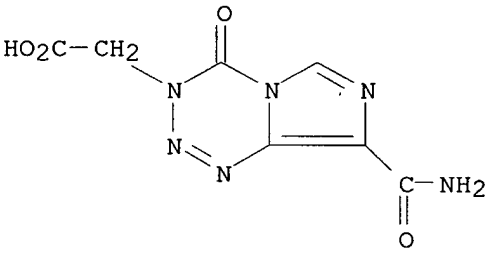
temozolomide (II) (26%) whereas deprotection of I [R = CH2SiMe3] with TBAF in acetonitrile-acetic acid gives 78% II. I [R = CH2Ph, CH2C6H4OMe-4, CHPh2] are stable to hydrogenolytic or oxidative debenzylation reactions.

IT **157466-97-2P 157466-98-3P 157466-99-4P**
157467-00-0P 172988-50-0P 172988-51-1P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**
(Preparation)
(prepn. of temozolomide and related imidazotetrazines using masked Me isocyanates)

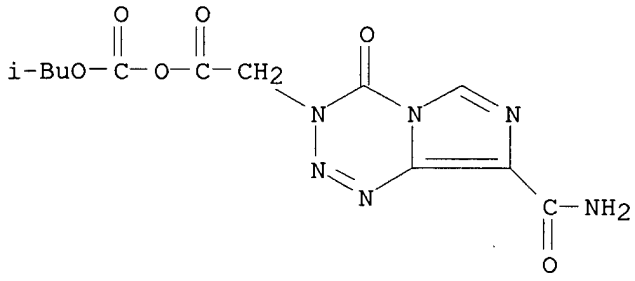
RN 157466-97-2 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-3(4H)-acetic acid, 8-(aminocarbonyl)-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



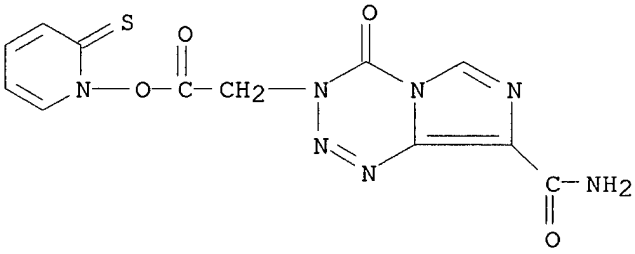
RN 157466-98-3 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-3(4H)-acetic acid, 8-(aminocarbonyl)-4-oxo- (9CI) (CA INDEX NAME)



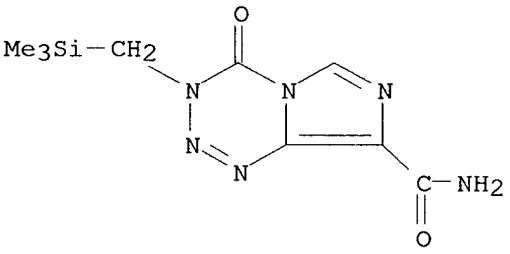
RN 157466-99-4 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-3(4H)-acetic acid, 8-(aminocarbonyl)-4-oxo-, anhydride with 2-methylpropyl hydrogen carbonate (9CI) (CA INDEX NAME)



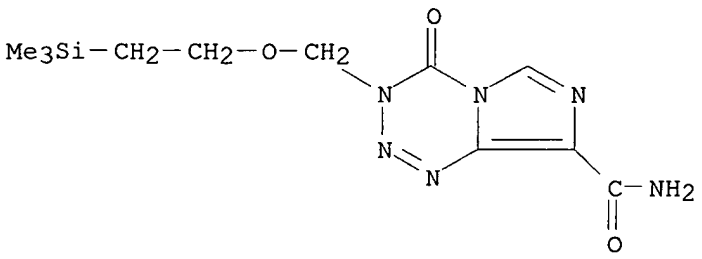
RN 157467-00-0 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-[2-oxo-2-[(2-thioxo-1(2H)-pyridinyl)oxy]ethyl]- (9CI) (CA INDEX NAME)



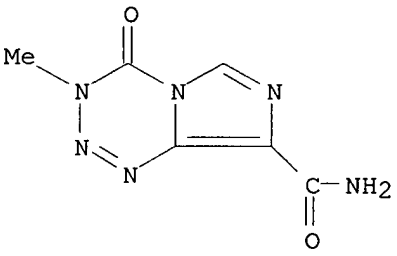
RN 172988-50-0 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-[(trimethylsilyl)methyl]- (9CI) (CA INDEX NAME)



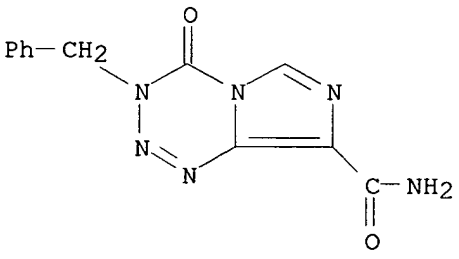
RN 172988-51-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-[[2-(trimethylsilyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



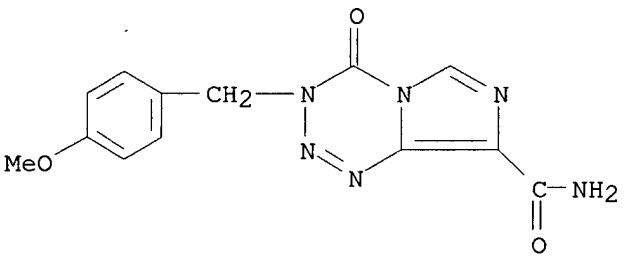
IT **85622-93-1P**, Temozolomide **85623-02-5P**
85623-05-8P 172988-48-6P 172988-49-7P
172988-52-2P
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of temozolomide and related imidazotetrazines using masked Me isocyanates)
RN 85622-93-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



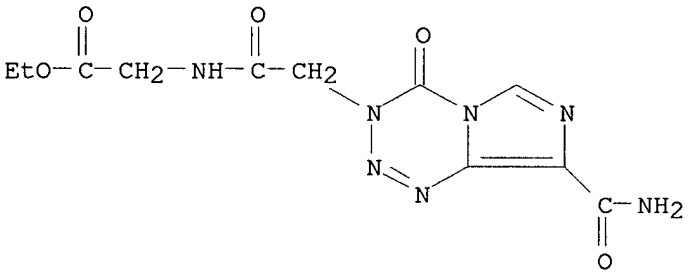
RN 85623-02-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



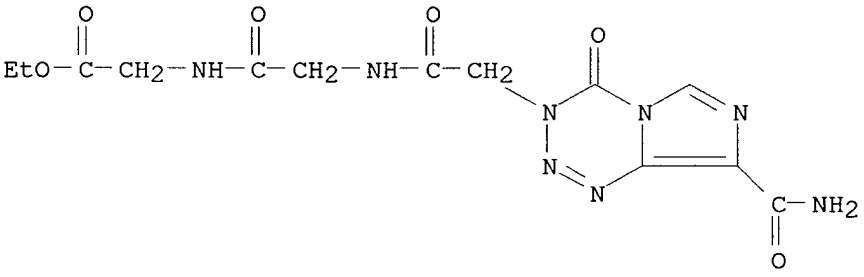
RN 85623-05-8 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-[(4-methoxyphenyl)methyl]-4-oxo- (9CI) (CA INDEX NAME)



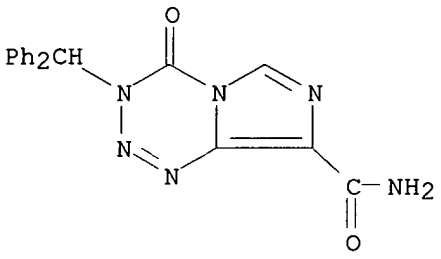
RN 172988-48-6 CAPLUS
CN Glycine, N-[[8-(aminocarbonyl)-4-oxoimidazo[5,1-d]-1,2,3,5-tetrazin-3(4H)-yl]acetyl]-, ethyl ester (9CI) (CA INDEX NAME)



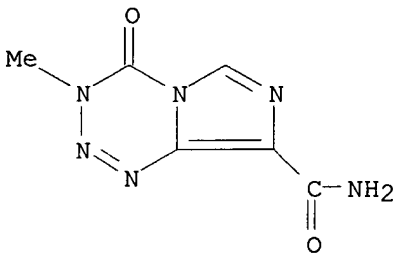
RN 172988-49-7 CAPLUS
CN Glycine, N-[[[8-(aminocarbonyl)-4-oxoimidazo[5,1-d]-1,2,3,5-tetrazin-3(4H)-yl]acetyl]glycyl]-, ethyl ester (9CI) (CA INDEX NAME)



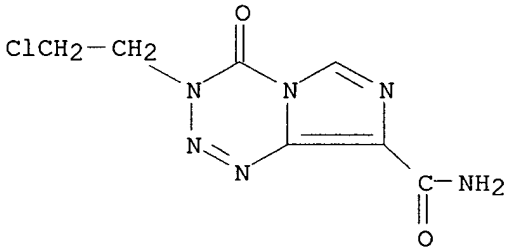
RN 172988-52-2 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(diphenylmethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



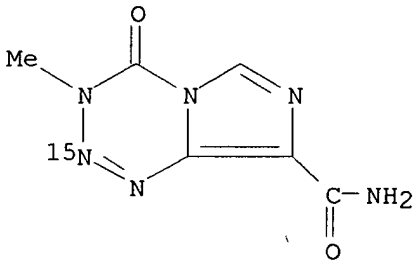
L6 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1995:508250 CAPLUS
DN 123:198751
TI Antitumor Imidazotetrazines. 32.1 Synthesis of Novel Imidazotetrazinones and Related Bicyclic Heterocycles To Probe the Mode of Action of the Antitumor Drug Temozolomide
AU Clark, A. S.; Deans, B.; Stevens, M. F. G.; Tisdale, M. J.; Wheelhouse, R. T.; Denny, B. J.; Hartley, J. A.
CS Pharmaceutical Sciences Institute, Aston University, Birmingham, B4 7ET, UK
SO J. Med. Chem. (1995), 38(9), 1493-504
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
AB A series of new imidazo[5,1-d]-1,2,3,5-tetrazinones with addnl. hydrogen-bonding or ionic substituents at the 8-carboxamide position of the antitumor drugs temozolomide and mitozolomide were prepd. None of these compds. were significantly more cytotoxic in vitro against the mouse TLX5 lymphoma than the lead structures. Mol. modeling techniques were used to design benzo- and pyrazolo[4,3-d]-1,2,3-triazinones bearing carboxamide groups in appropriate positions which are isosteric with temozolomide and mitozolomide but which cannot ring open to alkylating species. As predicted, these compds. have no inhibitory properties against human GM892A or Raji cell lines in vitro. Temozolomide and the spermidine-temozolomide conjugate 28 preferentially methylate guanines within guanine-rich sequences in DNA, but no exptl. evidence has been found to support the hypothesis that such regions are involved in catalyzing the ring opening of the imidazotetrazinone prodrugs to their active forms.
IT **85622-93-1DP**, Temozolomide, derivs. **85622-95-3DP**, Mitozolomide, derivs.
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(prepn. of imidazotetrazinones as probes for action of temozolomide)
RN 85622-93-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



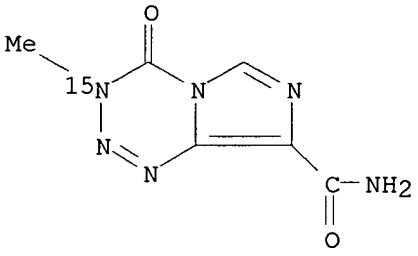
RN 85622-95-3 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



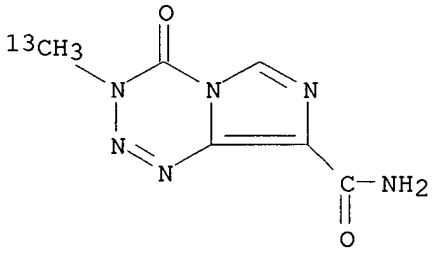
L6 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1995:374136 CAPLUS
DN 122:214043
TI Antitumor imidazotetrazines. Part 31. The synthesis of isotopically labeled temozolomide and a multinuclear (1H, 13C, 15N) magnetic resonance investigation of temozolomide and mitozolomide
AU Wheelhouse, Richard T.; Wilman, Derry E. V.; Thomson, William; Stevens, Malcolm F. G.
CS Cancer Res. Laboratories, Univ. Nottingham, Nottingham, NG7 2RD, UK
SO J. Chem. Soc., Perkin Trans. 1 (1995), (3), 249-52
CODEN: JCPRB4; ISSN: 0300-922X
DT Journal
LA English
OS CASREACT 122:214043
AB The antitumor drug temozolomide has been synthesized isotopically labeled with NMR active nuclei at a variety of sites and all its 13C and 15N NMR spectral resonances have been assigned. At low pH a site of protonation has been identified which accounts for the acid stability of the drug.
IT **162021-24-1P 162021-28-5P 162021-29-6P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(synthesis of isotopically labeled temozolomide and a multinuclear magnetic resonance investigation of temozolomide and mitozolomide)
RN 162021-24-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-2-15N-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



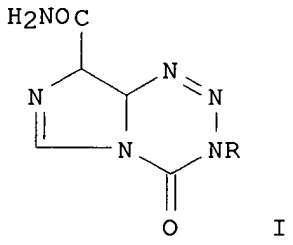
RN 162021-28-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-3-15N-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



RN 162021-29-6 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-(methyl-13C)-4-oxo- (9CI) (CA INDEX NAME)



L6 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1994:557614 CAPLUS
DN 121:157614
TI Alternative syntheses of the antitumor drug temozolomide avoiding the use of methyl isocyanate
AU Wang, Yongfeng; Stevens, Malcolm F. G.; Thomson, W.
CS Cancer Res. Lab., Univ. Nottingham, Nottingham, NG7 2RD, UK
SO J. Chem. Soc., Chem. Commun. (1994), (14), 1687-8
CODEN: JCCCAT; ISSN: 0022-4936
DT Journal
LA English
OS CASREACT 121:157614
GI



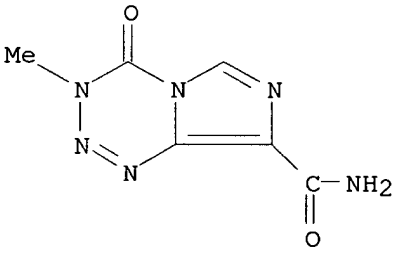
I

AB Et (8-carbamoyl-3,4-dihydro-4-oxoimidazo[5,1-d]-1,2,3,5-tetrazin-3-yl)acetate (I, R = CH2CO2Et) can be prepd. by two routes starting from 5-aminoimidazole-4-carboxamide; hydrolysis of I (R = CH2CO2Et) to the corresponding carboxylic acid followed by Barton radical decarboxylation gives the antitumor imidazotetrazinone temozolomide (I, R = Me).

IT **85622-93-1P**, Temozolomide
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(alternative synthesis of)

RN 85622-93-1 CAPLUS

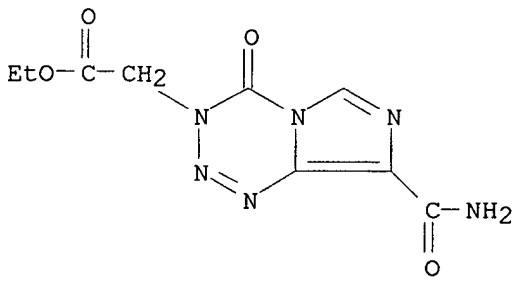
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



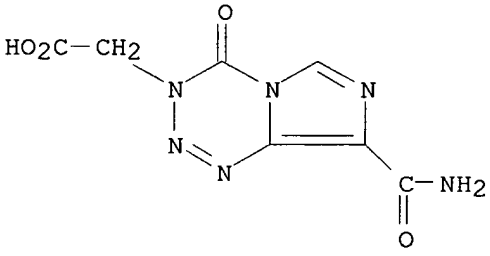
IT **157466-97-2P 157466-98-3P 157466-99-4P 157467-00-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. and reaction of, in synthesis of temozolomide)

RN 157466-97-2 CAPLUS

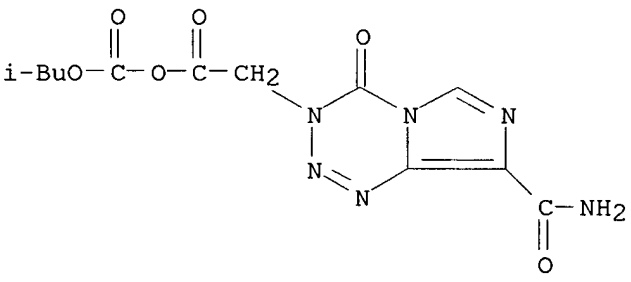
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-3(4H)-acetic acid, 8-(aminocarbonyl)-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)



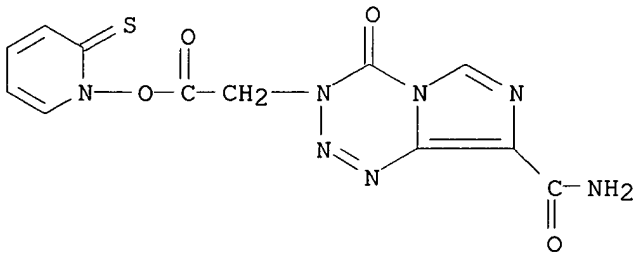
RN 157466-98-3 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-3(4H)-acetic acid, 8-(aminocarbonyl)-4-oxo- (9CI) (CA INDEX NAME)



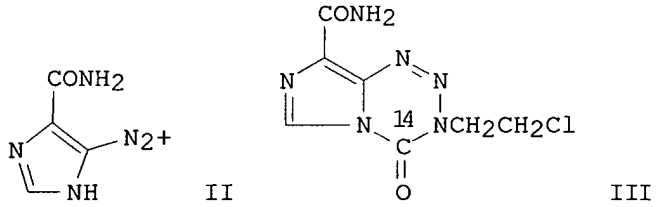
RN 157466-99-4 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-3(4H)-acetic acid, 8-(aminocarbonyl)-4-oxo-, anhydride with 2-methylpropyl hydrogen carbonate (9CI) (CA INDEX NAME)



RN 157467-00-0 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-[2-oxo-2-[(2-thioxo-1(2H)-pyridinyl)oxy]ethyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1989:94466 CAPLUS
DN 110:94466
TI Carbon-14 labeling of 2-chloroethyl isocyanate. Application to the labeling of (chloroethyl)tetrazinone and (chloroethyl)nitrosoureas
AU Madelmont, J. C.; Moreau, M. F.; Godeneche, D.; Labarre, P.; Veyre, A.
CS INSERM, Clermont-Ferrand, 63005, Fr.
SO J. Labelled Compd. Radiopharm. (1988), 25(10), 1135-42
CODEN: JLCRD4; ISSN: 0362-4803
DT Journal
LA French
OS CASREACT 110:94466
GI

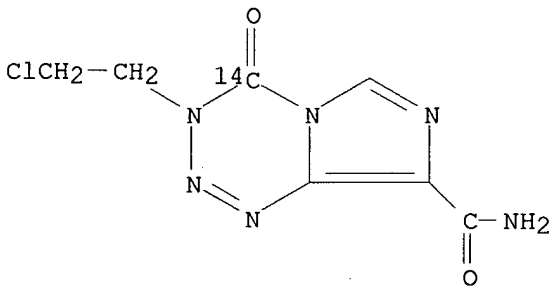


II III

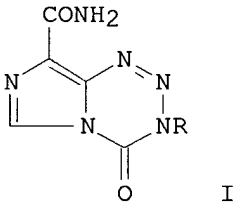
AB Isocyanate ClCH2CH2N14CO (I) was prepd. from ClCH2CH214CO2H via the acyl azide. I was converted to an aryl carbamate, and subsequent nitrosation, amidation (MeSCH2CH2NH2), and oxidn. gave ureas MeS(O)nCH2CH2NH14CON(NO)CH2CH2Cl (n = 1, 2). The reaction of I with imidazolediazonium compd. II gave 14C-labeled mitozolomide (III).

IT- **118971-95-2P**
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of)

RN 118971-95-2 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-4-14C-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



L6 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1988:68357 CAPLUS
DN 108:68357
TI Antitumor activity and pharmacokinetics in mice of 8-carbamoyl-3-methylimidazo[5,1-d]-1,2,3,5-tetrazin-4(3H)-one (CCRG 81045; M & B 39831), a novel drug with potential as an alternative to dacarbazine
AU Stevens, Malcolm F. G.; Hickman, John A.; Langdon, Simon P.; Chubb, David; Vickers, Lisa; Stone, Robert; Baig, Ghousia; Goddard, Colin; Gibson, Neil W.; et al.
CS Pharm. Sci. Inst., Aston Univ., Birmingham, B4 7ET, UK
SO Cancer Res. (1987), 47(22), 5846-52
CODEN: CNREA8; ISSN: 0008-5472
DT Journal
LA English
GI



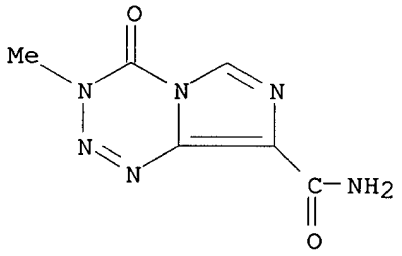
I

AB A no. of 3-alkyl analogs [I, e.g., R = Me, Et, (CH2)2Br, or Pr] of the exptl. antitumor drug mitozolomide [I, R = (CH2)2Cl] were screened against murine tumors in vivo. Only the compds. with a 3-methyl- or 3-bromoethyl group had significant antitumor activity against the TLX5 lymphoma. The 3-Me analog, CCRG 81045 (II) had good activity, when administered i.p., against L1210 and P388 leukemias, M5076 reticulum cell sarcoma, B16 melanoma, and ADJ/PC6A plasmacytoma. II was also active when administered orally to mice bearing the L1210 leukemia. A daily schedule of 100 mg/kg II for 5 days produced increases of survival time of treated animals compared to controls of 176 and >235% against the P388 and L1210 leukemias, resp. In the female C57BL .times. DBA/2 F1 mouse the 10% LD was 125 mg/kg daily for 5 days. II underwent mild alk. hydrolysis and ring fission to form the linear triazene, 5-(3-methyltriazen-1-yl)imidazole-4-carboxamide (III), which is the putative metabolite formed upon metabolic activation of the antitumor drug dacarbazine [5-(3,3-dimethyltriazen-1-yl)imidazole-4-carboxamide]. The half-life of II at 37.degree. in 0.2M phosphate buffer (pH 7.4) was 1.24 h, whereas

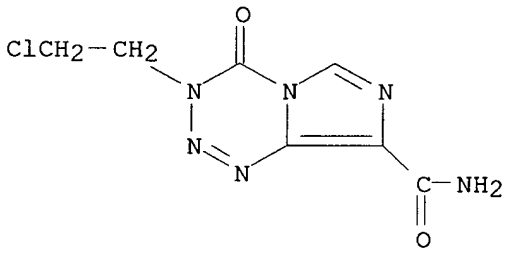
that of III at 25.degree. was 8 min. The half-life of II in human plasma in vitro at 37.degree. was 0.42 h. Pharmacokinetic expts. conducted in BALB/c mice produced plasma profiles of II, administered i.p. or orally, which showed a rapid absorption phase, elimination half-lives of 1.13 h (i.p.) and 1.29 h (oral) and a bioavailability of 0.98.

IT **85622-93-1P**, CCRG 81045 **85622-95-3P**, Mitozolomide
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. and antitumor activity and pharmacokinetics of)

RN 85622-93-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)

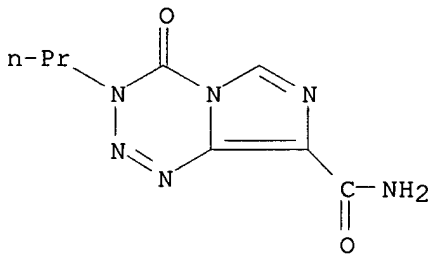


RN 85622-95-3 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)

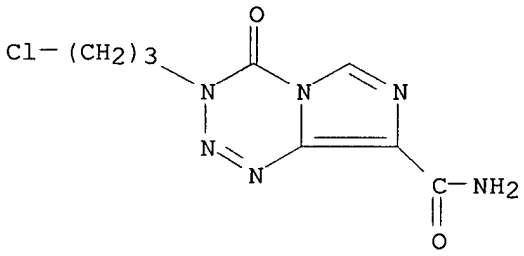


IT **85622-94-2P 85622-97-5P 85622-98-6P**
85622-99-7P 85623-01-4P 85623-02-5P
85623-03-6P 97716-74-0P 108030-65-5DP, derivs.
112557-08-1P 112557-09-2P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(prepn. and antitumor activity of)

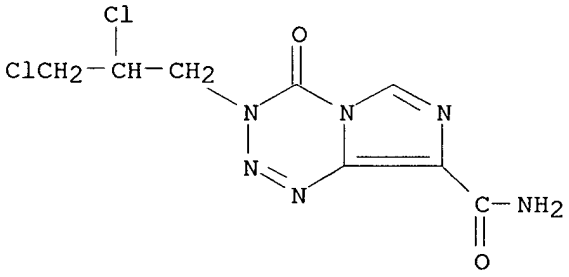
RN 85622-94-2 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-propyl- (9CI) (CA INDEX NAME)



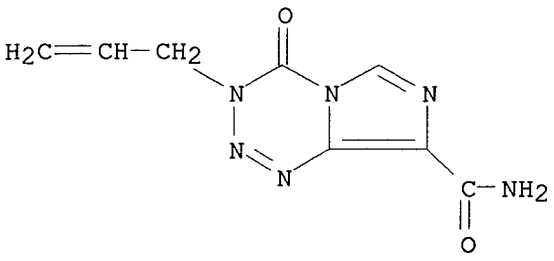
RN 85622-97-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(3-chloropropyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



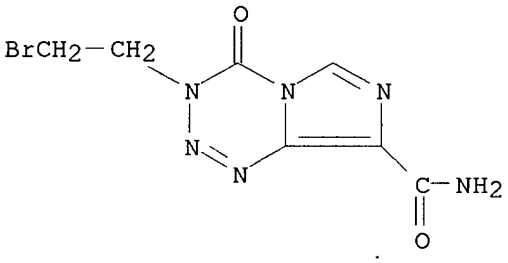
RN 85622-98-6 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2,3-dichloropropyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



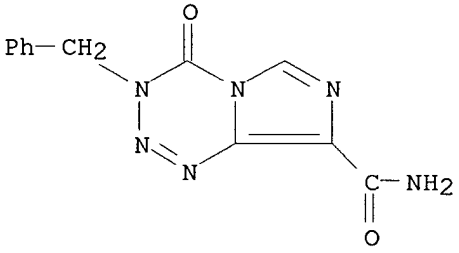
RN 85622-99-7 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-(2-propenyl)- (9CI) (CA INDEX NAME)



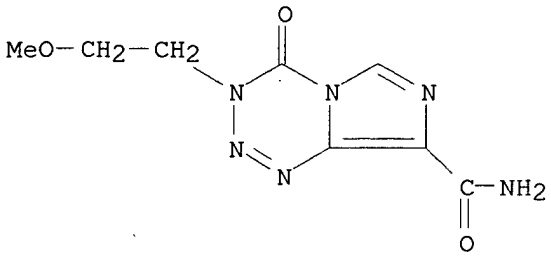
RN 85623-01-4 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-bromoethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



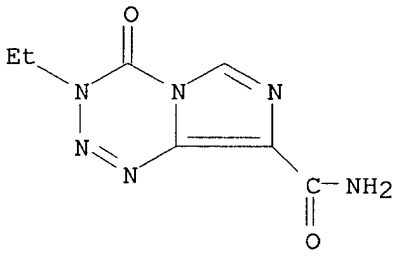
RN 85623-02-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



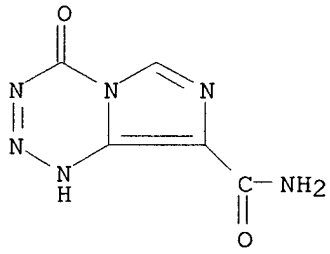
RN 85623-03-6 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-(2-methoxyethyl)-4-oxo- (9CI) (CA INDEX NAME)



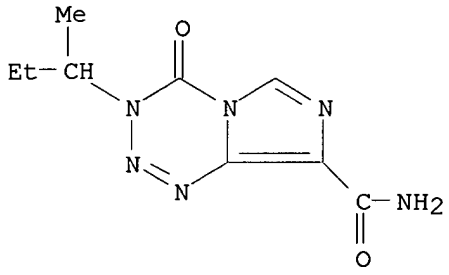
RN 97716-74-0 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-ethyl-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



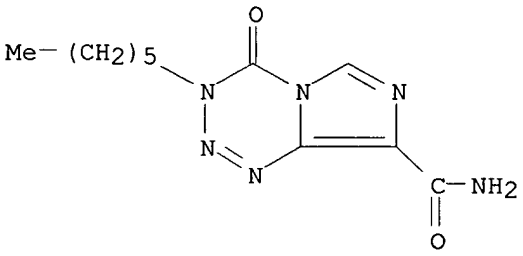
RN 108030-65-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 1,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



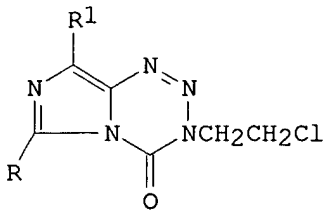
RN 112557-08-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-(1-methylpropyl)-4-oxo- (9CI) (CA INDEX NAME)



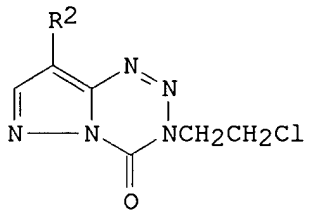
RN 112557-09-2 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-hexyl-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



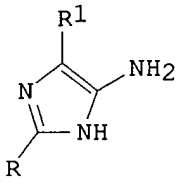
L6 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1987:102242 CAPLUS
DN 106:102242
TI Antitumor imidazotetrazines. 14. Synthesis and antitumor activity of 6- and 8-substituted imidazo[5,1-d]-1,2,3,5-tetrazinones and 8-substituted pyrazolo[5,1-d]-1,2,3,5-tetrazinones
AU Lunt, Edward; Newton, Christopher G.; Smith, Christopher; Stevens, Graham P.; Stevens, Malcolm F. G.; Straw, Colin G.; Walsh, Roger J. A.; Warren, Peter J.; Fizames, Christian; et al.
CS Res. Inst., May and Baker Ltd., Dagenham/Essex, RM10 7XS, UK
SO J. Med. Chem. (1987), 30(2), 357-66
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
OS CASREACT 106:102242
GI



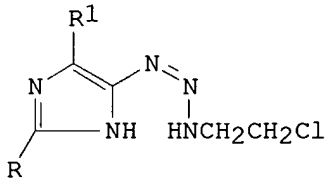
I



II



IV



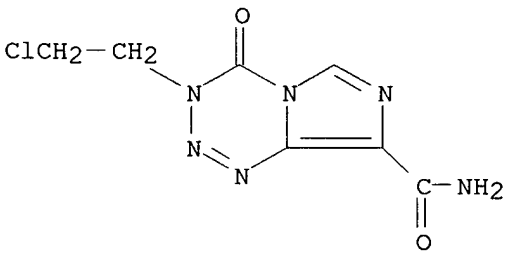
V

AB Imidazo[5,1-d]-1,2,3,5-tetrazinones I (R = alkyl or aralkyl, R1 = CONH2; R = H, R1 = CONHMe, CONMe2, CN, SO2Me, SO2NHMe, etc.) and pyrazolo[5,1-d]-1,2,3,5-tetrazinones II (R2 = CONH2, CONMe2, NO2, SO2Me) were prepd. as derivs. of the antitumor agent mitozolomide (I; R = H, R1 = CONH2) (III). Thus, imidazoles IV were diazotized and the cyclized with ClCH2CH2NCO to give the corresponding I. I (R = alkyl or aralkyl, R1 = CONH2) showed optimal antitumor activity when the group was small or linear, but activity diminished as size and branching of this substituent increased. This may reflect altered transport characteristics, or failure of the enlarged derivs. to fit a binding site, or possibly a reduced tendency for the derivs. having bulky groups at position 6 to hydrolytically generate the putatively active triazenes V. Testing of 14 derivs. of III substituted differently at position 8 revealed a complex structure-activity relationship, with good antitumor activity obtained for carbamoyl and sulfamoyl groups bearing small substituents. The 8-methylsulfonyl compd. had noteworthy activity, but the 8-cyano, 8-nitro, and 8-Ph derivs. were devoid of useful antitumor activity.

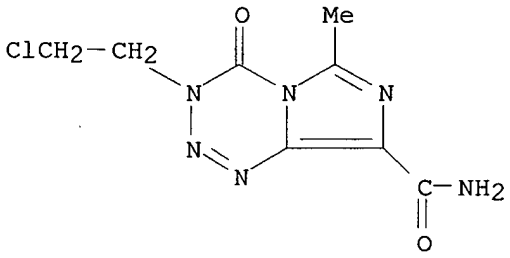
IT **85622-95-3DP**, Mitozolomide, derivs. **90521-16-7P 90521-26-9P 90521-27-0P 90521-28-1P 90521-29-2P 90521-30-5P 90521-31-6P 90521-32-7P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(prepn. and antitumor activity of)

RN 85622-95-3 CAPLUS

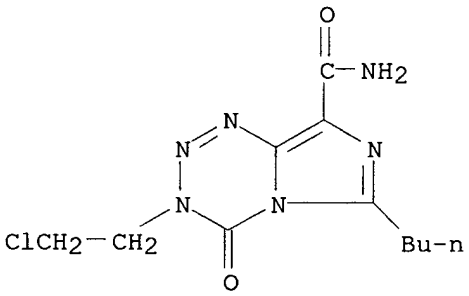
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



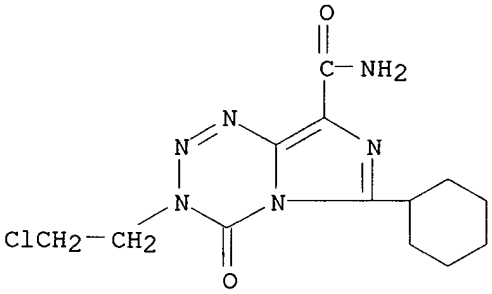
RN 90521-16-7 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-6-methyl-4-oxo- (9CI) (CA INDEX NAME)



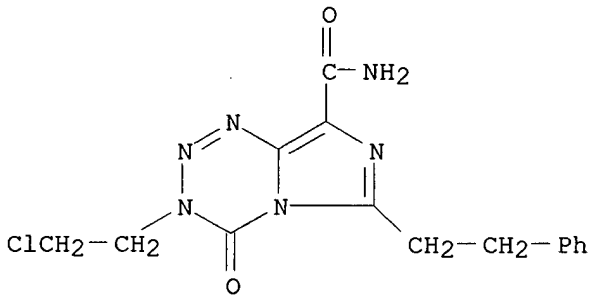
RN 90521-26-9 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 6-butyl-3-(2-chloroethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



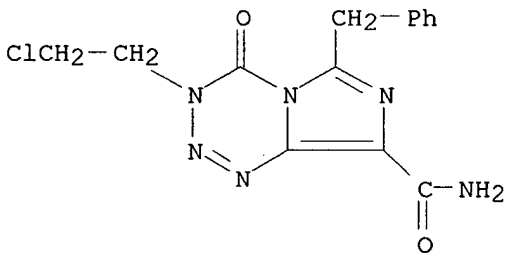
RN 90521-27-0 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-6-cyclohexyl-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



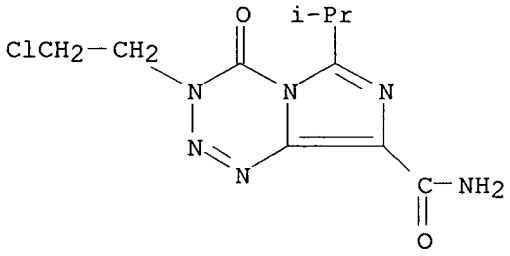
RN 90521-28-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo-6-(2-phenylethyl)- (9CI) (CA INDEX NAME)



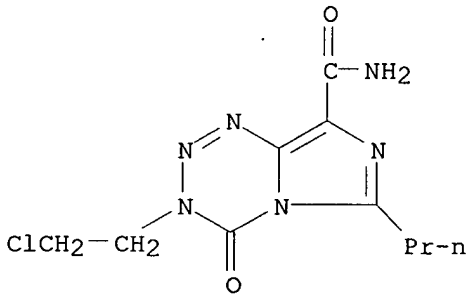
RN 90521-29-2 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo-6-(phenylmethyl)- (9CI) (CA INDEX NAME)



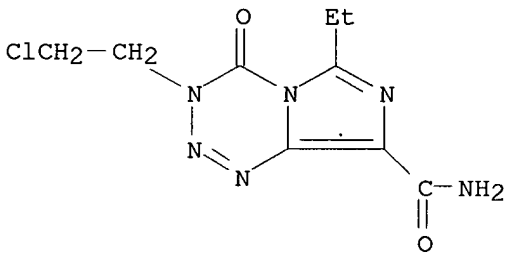
RN 90521-30-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-6-(1-methylethyl)-4-oxo- (9CI) (CA INDEX NAME)



RN 90521-31-6 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo-6-propyl- (9CI) (CA INDEX NAME)



RN 90521-32-7 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-6-ethyl-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



L6 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1984:423509 CAPLUS
DN 101:23509
TI Tetrazine derivatives
IN Baig, Ghouse Unissa; Stevens, Malcolm Francis Graham; Lunt, Edward; Newton, Christopher Gregory; Pedgrift, Brian Leslie; Smith, Christopher; Straw, Colin Geoffrey; Walsh, Roger John Aitchison; Warren, Peter James
PA May and Baker Ltd., UK
SO Ger. Offen., 74 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3329505	A1	19840223	DE 1983-3329505	19830816
	FR 2531958	A1	19840224	FR 1983-13246	19830812
	FR 2531958	B1	19861031		
	SE 8304415	A	19840218	SE 1983-4415	19830815
	SE 455198	B	19880627		
	SE 455198	C	19881006		
	FI 8302927	A	19840218	FI 1983-2927	19830815
	FI 80273	B	19900131		
	FI 80273	C	19900510		
	AU 8317968	A1	19840223	AU 1983-17968	19830815
	AU 575782	B2	19880811		
	GB 2125402	A1	19840307	GB 1983-21942	19830815
	GB 2125402	B2	19851113		

	NL 8302863	A	19840316	NL 1983-2863	19830815
	HU 31735	O	19840528	HU 1983-2860	19830815
	HU 189321	B	19860630		
	ZA 8306003	A	19840725	ZA 1983-6003	19830815
	IL 69500	A1	19890131	IL 1983-69500	19830815
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	DK 8303749	A	19840218	DK 1983-3749	19830816
	AT 8302942	A	19911115	AT 1983-2942	19830816
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	JP 59053488	A2	19840328	JP 1983-149273	19830817
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	CH 657855	A	19860930	CH 1983-4490	19830817
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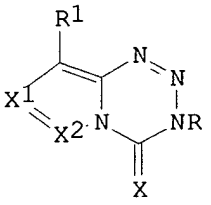
	GB 1982-23583		19820817		
	GB 1982-26169		19820914		
	GB 1983-6904		19830314		
	GB 1982-23483		19820817		

OS CASREACT 101:23509

GI



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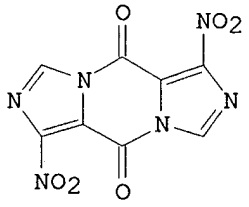

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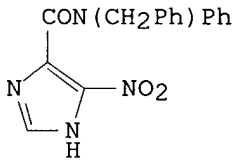


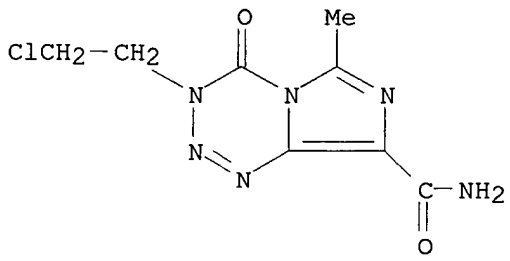
III

AB Antineoplastic (no data) azolotetrazolines I [R = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl; R1 = R2S(O)n, sulfamoyl, carbamoyl, acyl, etc.; R2 = alkyl, alkenyl; n = 0-2; X = O, S; X1 or X2 = N, the other = CR3; R3 = H, halo, cyano, OH, NO2, (un)substituted alkyl, alkenyl, Ph, PhO, acyl, etc.] were prepd. Thus, 5-nitro-1H-imidazole-4-carboxylic acid was self-cyclocondensed by heating with PCl5 to give diimidazopyrazinedione II. This was treated with PhCH2NHPh to give imidazolecarboxamide III.HCl, which was hydrogenated to the amine, condensed with NaN3 to give the 5-diazo deriv., and cyclocondensed with MeNCO to give I [R = Me, R1 = CON(CH2Ph)Ph, X, = O, X1 = CH, X2 = N].

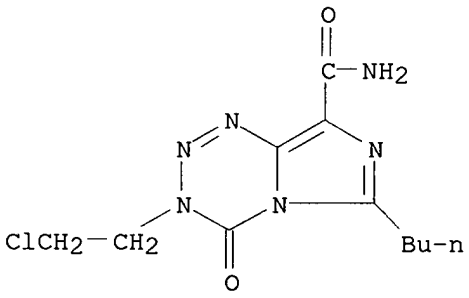
IT **90521-16-7P 90521-26-9P 90521-27-0P**
90521-28-1P 90521-29-2P 90521-30-5P
90521-31-6P 90521-32-7P
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of)

RN 90521-16-7 CAPLUS

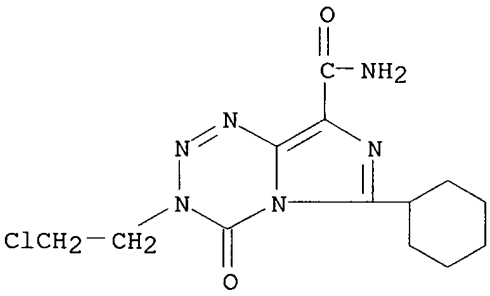
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-6-methyl-4-oxo- (9CI) (CA INDEX NAME)



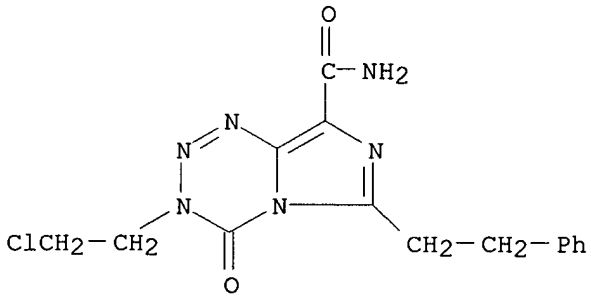
RN 90521-26-9 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 6-butyl-3-(2-chloroethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



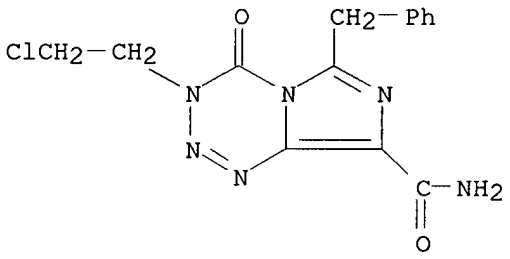
RN 90521-27-0 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-6-cyclohexyl-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



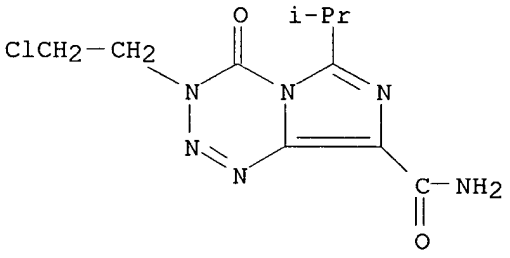
RN 90521-28-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo-6-(2-phenylethyl)- (9CI) (CA INDEX NAME)



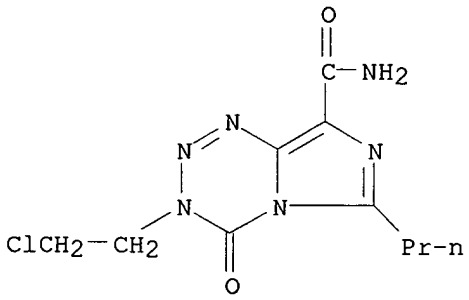
RN 90521-29-2 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo-6-(phenylmethyl)- (9CI) (CA INDEX NAME)



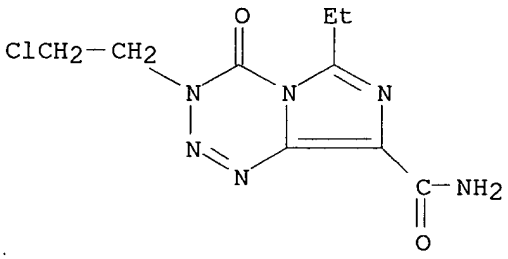
RN 90521-30-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-6-(1-methylethyl)-4-oxo- (9CI) (CA INDEX NAME)



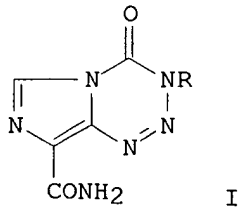
RN 90521-31-6 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo-6-propyl- (9CI) (CA INDEX NAME)



RN 90521-32-7 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-6-ethyl-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



L6 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1984:51553 CAPLUS
DN 100:51553
TI Antitumour imidazotetrazines. 1. Synthesis and chemistry of 8-carbamoyl-3-(2-chloroethyl)imidazo[5,1-d]-1,2,3,5-tetrazin-4(3H)-one, a novel broad-spectrum antitumor agent
AU Stevens, Malcolm F. G.; Hickman, John A.; Stone, Robert; Gibson, Neil W.; Baig, Ghouse Unissa; Lunt, Edward; Newton, Christopher G.
CS Dep. Pharm., Univ. Aston, Birmingham, B4 7ET, UK
SO J. Med. Chem. (1984), 27(2), 196-201
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI



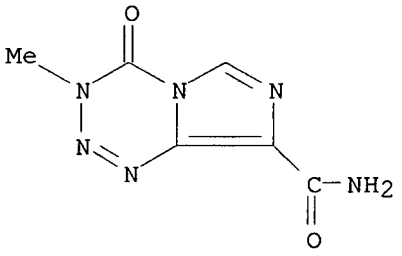
I

AB Interaction of 5-diazo-4-imidazolecarboxamide and alkyl and aryl isocyanates in the dark gave 8-carbamoylimidazo[5,1-d]-1,2,3,5-tetrazin-

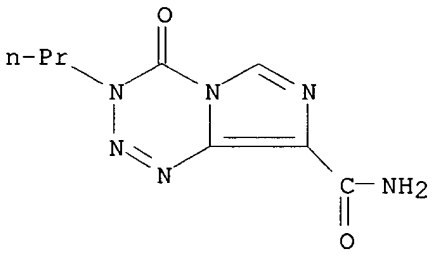
4(3H)-ones (I). In cold MeOH or EtOH, I (R = ClCH2CH2; II) decompd to give 2-azahypoxanthine and ClCH2CH2NHCO2R (R = Me, Et). II was active against L-1210 and P388 leukemia and may act as a prodrug modification of the acyclic triazene 5-[3-(2-chloroethyl)traizen-1-yl]imidazole-4-carboxamide (MCTIC), since it underwent ring opening to form the triazene in aq. Na2CO3.

IT **85622-93-1P 85622-94-2P 87597-51-1P**
87597-52-2P 87597-53-3P 87597-54-4P
87597-55-5P 87597-56-6P 87597-57-7P
87597-58-8P
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**
(Preparation)
(prepn. and decompn. of)

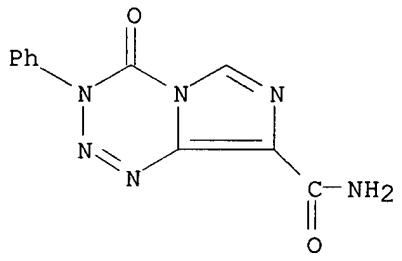
RN 85622-93-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



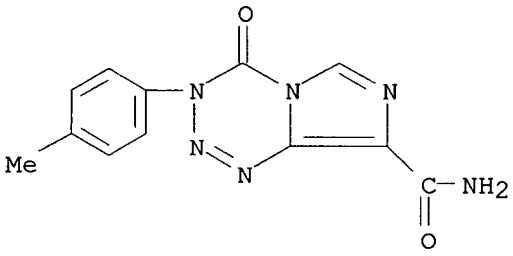
RN 85622-94-2 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-propyl- (9CI) (CA INDEX NAME)



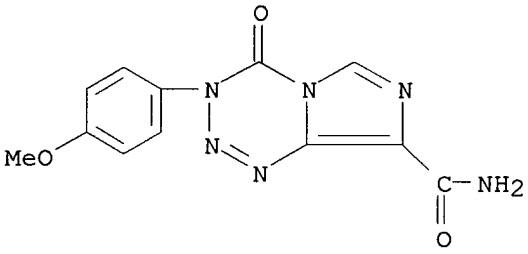
RN 87597-51-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-phenyl- (9CI) (CA INDEX NAME)



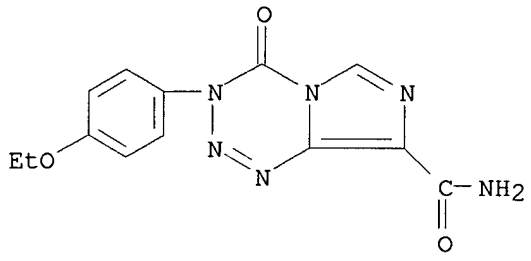
RN 87597-52-2 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-(4-methylphenyl)-4-oxo- (9CI) (CA INDEX NAME)



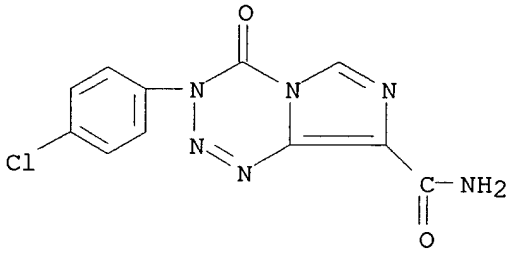
RN 87597-53-3 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-(4-methoxyphenyl)-4-oxo- (9CI) (CA INDEX NAME)



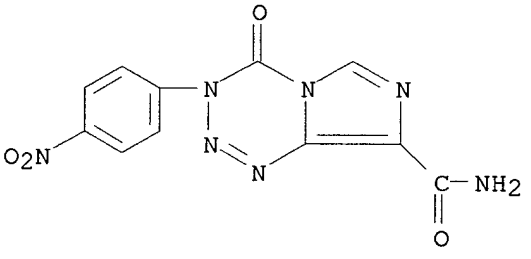
RN 87597-54-4 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(4-ethoxyphenyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



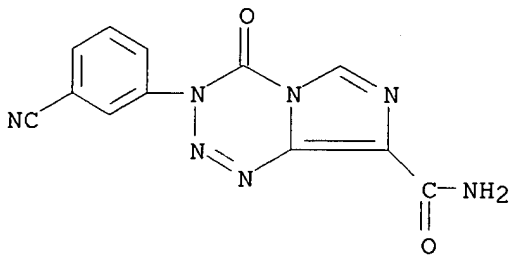
RN 87597-55-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(4-chlorophenyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



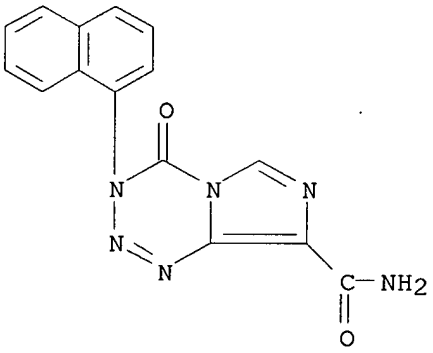
RN 87597-56-6 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-(4-nitrophenyl)-4-oxo- (9CI) (CA INDEX NAME)



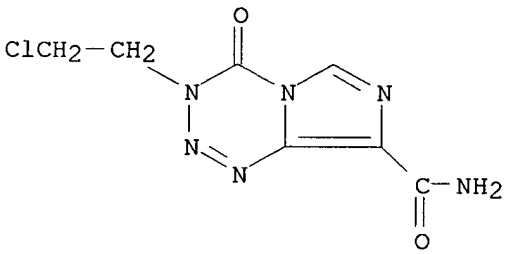
RN 87597-57-7 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(3-cyanophenyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



RN 87597-58-8 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-(1-naphthalenyl)-4-oxo- (9CI) (CA INDEX NAME)



IT **85622-95-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); **PREP (Preparation)**
(prepn., degrdn., and antitumor activity of)
RN 85622-95-3 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



L6 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2002 ACS
AN 1983:198285 CAPLUS
DN 98:198285
TI Tetrazine derivatives and pharmaceutical compositions containing them
IN Lunt, Edward; Stevens, Malcolm Francis Graham; Stone, Robert; Wooldridge, Kenneth Robert Harry

V. Balasubramanian

PA May and Baker Ltd., UK
SO Ger. Offen., 29 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3231255	A1	19830303	DE 1982-3231255	19820823
	DE 3231255	C2	19920227		
	IL 66606	A1	19870731	IL 1982-66606	19820812
	BE 894175	A1	19830223	BE 1982-208860	19820823
	DK 8203778	A	19830225	DK 1982-3778	19820823
	DK 161147	B	19910603		
	DK 161147	C	19911118		
	FI 8202921	A	19830225	FI 1982-2921	19820823
	FI 73434	B	19870630		
	FI 73434	C	19871009		
	FR 2511679	A1	19830225	FR 1982-14461	19820823
	FR 2511679	B1	19850201		
	SE 8204817	A	19830225	SE 1982-4817	19820823
	SE 448543	B	19870302		
	SE 448543	C	19870611		
	AU 8287493	A1	19830303	AU 1982-87493	19820823
	AU 571430	B2	19880421		
	GB 2104522	A1	19830309	GB 1982-24155	19820823
	GB 2104522	B2	19850612		
	JP 58043975	A2	19830314	JP 1982-144902	19820823
	JP 04005029	B4	19920130		
	NL 8203286	A	19830316	NL 1982-3286	19820823
	NL 192739	B	19970901		
	NL 192739	C	19980106		
	ZA 8206120	A	19830727	ZA 1982-6120	19820823
	ES 515176	A1	19831101	ES 1982-515176	19820823
	HU 27908	O	19831128	HU 1982-2708	19820823
	HU 186107	B	19850628		
	AT 8203191	A	19850915	AT 1982-3191	19820823
	AT 380256	B	19860512		
	CA 1197247	A1	19851126	CA 1982-409950	19820823
	CH 655114	A	19860327	CH 1982-5007	19820823
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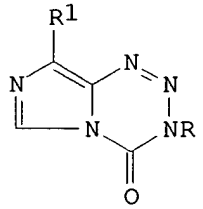

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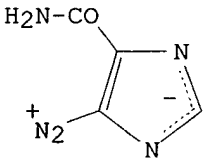
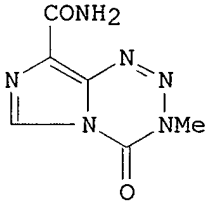


II



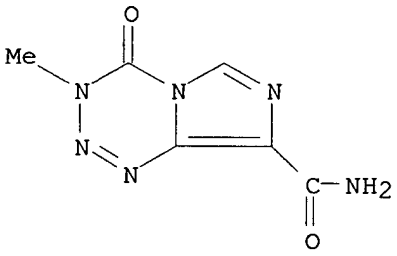
III

AB I [R = (un)substituted H, alkyl, alkenyl, alkynyl, aryl, cycloalkyl; R1 = (un)substituted carbamoyl] were prepd. as antitumor agents (no data). Thus, 500 mg II in 3.0 mL MeNCO were stirred in the dark 21 days to give

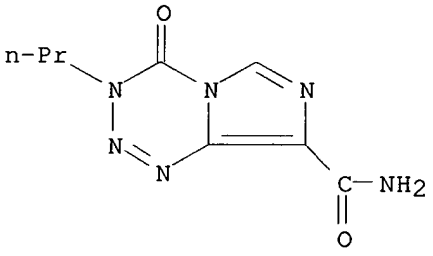
198 mg III.

IT **85622-93-1P 85622-94-2P 85622-95-3P**
85622-97-5P 85622-98-6P 85622-99-7P
85623-01-4P 85623-02-5P 85623-03-6P
85623-04-7P 85623-05-8P
RL: SPN (Synthetic preparation); **PREP (Preparation)**
(prepn. of)

RN 85622-93-1 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



RN 85622-94-2 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-propyl- (9CI) (CA INDEX NAME)



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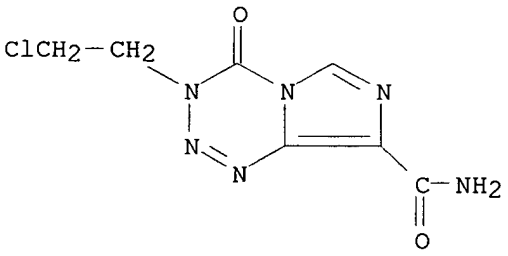
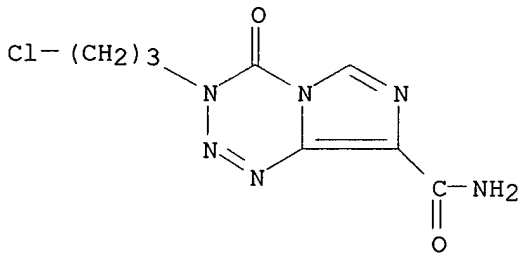
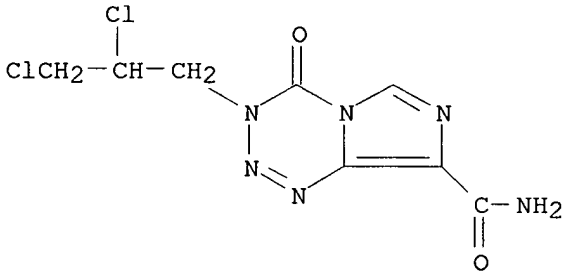
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-chloroethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



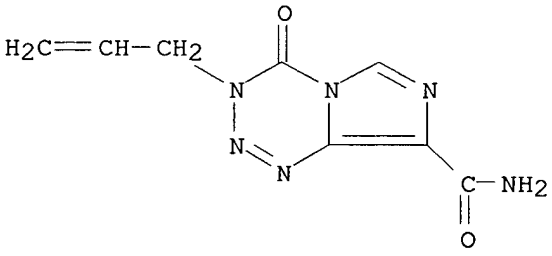
RN 85622-97-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(3-chloropropyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



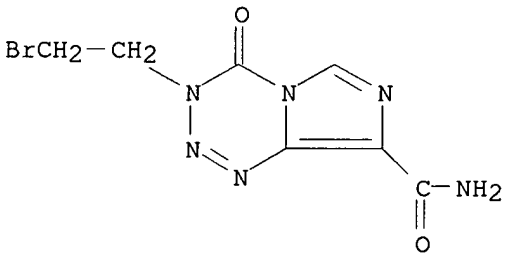
RN 85622-98-6 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2,3-dichloropropyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



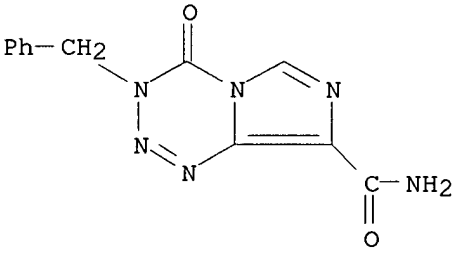
RN 85622-99-7 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-(2-propenyl)- (9CI) (CA INDEX NAME)



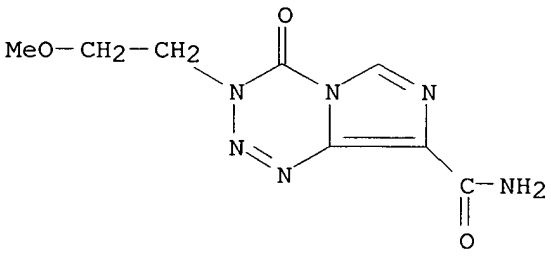
RN 85623-01-4 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-(2-bromoethyl)-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



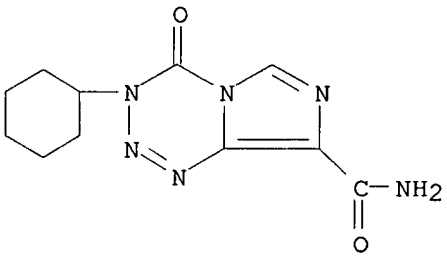
RN 85623-02-5 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-4-oxo-3-(phenylmethyl)- (9CI) (CA INDEX NAME)



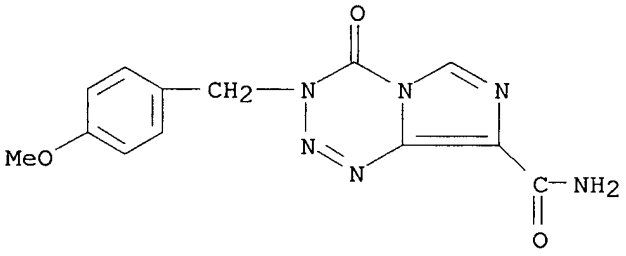
RN 85623-03-6 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-(2-methoxyethyl)-4-oxo- (9CI) (CA INDEX NAME)



RN 85623-04-7 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3-cyclohexyl-3,4-dihydro-4-oxo- (9CI) (CA INDEX NAME)



RN 85623-05-8 CAPLUS
CN Imidazo[5,1-d]-1,2,3,5-tetrazine-8-carboxamide, 3,4-dihydro-3-[(4-methoxyphenyl)methyl]-4-oxo- (9CI) (CA INDEX NAME)



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	77.43	220.20

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.53	-10.53

STN INTERNATIONAL LOGOFF AT 16:30:29 ON 06 MAY 2002